

In re Application of:  
Hall et al.  
Application No.: 09/441,966  
Filed: November 17, 1999  
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Patent  
Atty. Docket No.: AERO1120-1

### Amendments to the Claims

Please amend claims 1-10, 15 and 19 as indicated in the listing of claims.

Please cancel claim 22 without prejudice or disclaimer.

Please add new claims 23-25.

Claims 18, 20 and 21 and claims 11-14 were previously withdrawn or cancelled, respectively.

The listing of claims will replace all prior versions, and listings of claims in the application.

### Listing of Claims:

1. (Currently Amended) A method for accelerating the rate of mucociliary clearance in a subject in need thereof, comprising administering to the subject an effective mucociliary clearance stimulatory amount of a composition comprising a human Kunitz-type serine protease inhibitor and a physiologically acceptable carrier, wherein the human Kunitz-type serine protease inhibitor is SEQ ID NO:8~~selected from the group consisting of:~~

MAQLCGL RRSRAFLALL GSLLLLSGVLA	1
ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN	50
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF	100
NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE	150
ACMLRCFRQQ ENPPLPLGSK VVVLAGLFVM VLILFLGASM VYLIRVARRN	200
QERALRTVWS SGDDKEQLVK NTYVL	225

(SEQ ID NO.:49);<sub>3</sub>

AGSFLAWL GSLLLLSGVLA	1
ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN	50
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF	100
NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE	150
ACMLRCFRQQ ENPPLPLGSK VVVLAGAVS	179

(SEQ ID NO.:2);<sub>3</sub>

ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN	50
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF	100
NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE	150
ACMLRCFRQQ ENPPLPLGSK VVVLAGLFVM VLILFLGASM VYLIRVARRN	200
QERALRTVWS SGDDKEQLVK NTYVL	225

(SEQ ID NO.:45);<sub>3</sub>

MAQLCGL RRSRAFLALL GSLLLLSGVLA	1
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ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN — 50  
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF — 100  
NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE — 150  
ACMLRCFRQQ ENPPLPLGSK VVVLAGLFVM VLILFLGASM VYLIRVARRN — 200  
QERALRTVWS FGD — 213  
(SEQ ID NO.:47)<sub>32</sub>

ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN — 50  
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF — 100  
NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE — 150  
ACMLRCFRQQ ENPPLPLGSK VVVLAGLFVM VLILFLGASM VYLIRVARRN — 200  
QERALRTVWS SGDDKEQLVK NTYVL — 225  
(SEQ ID NO.:71)<sub>32</sub>

ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN — 50  
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF — 100  
NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE — 150  
ACMLRCFRQQ ENPPLPLGSK VVVLAGLFVM VLILFLGASM VYLIRVARRN — 200  
QERALRTVWS FGD — 213  
(SEQ ID NO.:70)<sub>32</sub>

IHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN — 50  
YLTKEECLKK CATV — 64  
(SEQ ID NO.:4)<sub>32</sub>

CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN — 50  
YLTKEECLKK C — 61  
(SEQ ID NO.:5)<sub>32</sub>

YEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE — 150  
ACMLRCFRQ — 159  
(SEQ ID NO.:6)<sub>32</sub>

CTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE — 150  
ACMLRC — 156  
(SEQ ID NO.:7)<sub>32</sub>

IHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN — 50  
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF — 100

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~~NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE~~ 150  
~~ACMLRCFRQ~~ 159  
~~(SEQ ID NO.:3);<sub>2</sub>~~

~~CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN~~ 50

~~YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF~~ 100  
~~NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE~~ 150  
~~ACMLRC~~ 156  
~~(SEQ ID NO.:50);<sub>2</sub>~~

~~ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN~~ 50

~~YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF~~ 100  
~~NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE~~ 150  
~~ACMLRCFRQQ ENPPLPLGSK VVVLGAVS~~ 179  
~~(SEQ ID NO.:1);<sub>2</sub>~~

~~ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN~~ 50  
~~YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF~~ 100  
~~NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE~~ 150  
~~ACMLRCFRQQ ENPPLPLGSK~~ 170  
~~(SEQ ID NO.:52);<sub>2</sub> and~~

~~ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN~~ 50

~~YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DS~~ 92

~~(SEQ ID NO.:8);~~

thereby accelerating the rate of mucociliary clearance.

2. (Currently amended) The method according to claim 1 ~~or 22~~, wherein the composition is administered to the lung airways.

3. (Currently amended) The method according to claim 1 ~~or 22~~, wherein said composition is administered directly by aerosolization.

4. (Currently amended) The method according to claim 1 ~~or 22~~, wherein said composition is administered directly as an aerosol ~~suspension~~ solution into the subject's respiratory tract.

5. (Currently amended) The method according to claim 4, wherein said aerosol ~~suspension~~ solution includes respirable particles ranging in size from about 1 to about 10 microns.

6. (Currently amended) The method according to claim 4, wherein said aerosol ~~suspension~~ solution includes respirable particles ranging in size from about 1 to about 5 microns.

7. (Currently amended) The method according to claim 4, wherein said aerosol ~~suspension~~ solution is delivered to said subject by a pressure driven nebulizer or administered as dry powder.

8. (Currently amended) The method according to claim 4, wherein said aerosol ~~suspension~~ solution is delivered to said subject by an ultrasonic nebulizer.

9. (Currently amended) The method according to claim 4, wherein said aerosol ~~suspension~~ solution is delivered to said subject by a non-toxic propellant.

10. (Currently amended) The method to claim 1 ~~or 22~~, wherein said carrier is a member selected from the group consisting of a physiologically buffered solution, an isotonic saline, normal saline, and combinations thereof.

11-14. (Canceled).

15. (Currently amended) The method according to claim 1 ~~or 22~~, wherein the human Kunitz-type serine protease inhibitor is

~~ADRERSIHDF-CLVSKVVGRC-RASMPRWWYN-VTDGSCQLFV-YGGCDGNSNN-50~~  
~~YLTKEECLKK-CATVTENATG-DLATSRNAAD-SSVPSAPRRQ-DS-92~~

(SEQ ID NO.:8).

16. (Previously presented) The method according to claim 1 or 15, wherein the human Kunitz-type serine protease inhibitor is glycosylated.

17. (Previously presented) The method according to claim 1 or 15, wherein the human Kunitz-type serine protease inhibitor contains at least one intra-chain cysteine-cysteine disulfide bond.

18. (Withdrawn) The method according to claim 1, wherein the Kunitz-type serine protease inhibitor contains at least one intra-chain cysteine-cysteine disulfide bond selected from the cysteine-cysteine paired groups consisting of CYS11-CYS61, CYS20-CYS44, CYS36-CYS57, CYS106-CYS156, CYS115-CYS139, and CYS131-CYS152 for any of SEQ ID NO.: 49, SEQ ID NO.: 2, SEQ ID NO.: 45, SEQ ID NO.: 47, SEQ ID NO.: 71, SEQ ID NO.: 70, SEQ ID NO.: 3, SEQ ID NO.: 50, SEQ ID NO.: 1, and SEQ ID NO.: 52, wherein the cysteine residues are numbered according to the amino acid sequence of SEQ ID NO.: 52.

19. (Currently amended) The method of claim 1 ~~or 22~~, wherein the human Kunitz-type serine protease inhibitor contains at least one intra-chain cysteine-cysteine disulfide bond selected from the cysteine-cysteine paired groups consisting of CYS11-CYS61, CYS20-CYS44, CYS36-CYS57, for ~~any of SEQ ID NO.: 4, SEQ ID NO.: 5, and~~ SEQ ID NO.: 8, wherein the cysteine residues are numbered according to the amino acid sequence of SEQ ID NO.: 52.

20. (Withdrawn) The method according to claim 1, wherein the Kunitz-type serine protease inhibitor contains at least one intra-chain cysteine-cysteine disulfide bond selected from the cysteine-cysteine paired groups consisting of CYS106-CYS156, CYS115-CYS139, and CYS131-CYS152 for any of SEQ ID NO.: 6, and SEQ ID NO.: 7, wherein the cysteine residues are numbered according to the amino acid sequence of SEQ ID NO.: 52.

21. (Withdrawn) The method according to claim 1, wherein the human Kunitz-type serine protease inhibitor contains at least one intra-chain cysteine-cysteine disulfide bond selected from the cysteine-cysteine paired groups consisting of CYS11-CYS61, CYS20-CYS44, CYS36-CYS57, wherein the cysteine residues are numbered according to the amino acid sequence of SEQ ID NO.: 52.

22. (Canceled).

23. (New) The method of claim 1, wherein the Kunitz-type serine protease inhibitor inhibits sodium channels.

24. (New) The method of claim 23, wherein the channel is an epithelial sodium channel.

25. (New) The method of claim 1, wherein Kunitz-type serine protease increases tracheal mucus velocity (TMV) in the subject.